July 11, 1945

Dr. Van R. Potter
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Madison, Wisconsin

Dear Van;

Thanks for your letter of July 6. I have followed your advice and am now composing a letter and suggested project for Dr. Schram's consideration which I hope to get off in the next day or so. In my letter to Dr. Schram I state my intentions of keeping in relatively close contact with your group for advice and counsel particularly in matters pertaining to the relations between the results obtained and the cancer problem.

Insofar as the cancer problem is concerned I have in mind to tackle the following question which seems to me to be one of the critical points at issue: Under what conditions can one of these self-duplicating units establish itself within the normal enzymatic population ? As you have clearly indicated in your publications it seems most probable that competitive interactions play an important role in determining the trend in enzymatic constitution within the cell. I believe that this question in its more general form is amenable to more or less direct analysis with the available techniques and material. At the very least I can hope to delineate with relative clarity the kinetics of the competition between two enzymes being formed simultaneously in the same cell. With the aid of this kind of data we should be able to provide a reasonably precise description of the conditions under which (in certain instances) a particular enzyme is successful in establishing itself within the cell and perhaps of even greater importance how to differentially prevent it from so doing.

In this connection it seems of more than passing interest to examine a series of carcinogens for their effect not only on simple enzyme formation but on the dynamics of the competition between two enzymes which are being induced and followed simultaneously. There are in general two ways to favor the formation of a particular enzyme; (a) to channel energy and precursor intiis direction (with substrate or by some other means); (b) to differentially suppress the synthetic activities of those enzymes with which it is in competition. Conceivably the examination of the effect of carcinogens on the formation of adaptive enzymes could help us to decide which of the above mechanisms are involved ~~which~~ a carcinogenic compound succeeds in altering the enzymatic consitution of a cell. In any case I think the question is important enough to warrant the attempt.

I would very much like to talk these experiments over with you in particular as concerns the compounds to be selected. I have been asked to write a review for Physiological Reviews on enzyme variation and its control and would like to include a section on your contributions in connection with the cancer question as a problem in the control of enzymatic constitution. I should also like to talk this over with you.

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It so happens that I must shortly go up to the University of Minnesota and I would like to drop off in Madison on my way back if and when you would be around. I am also rather anxious to see Dr. Meyer about the morphogenesis paper. I received a very kind letter from him expressing interest and the desire for another discussion. Drop me a line on when you will be around and I will arrange my trip accordingly. By the way, I would greatly appreciate it if you would include the Samuel references you mentioned in your last letter.

You will receive under separate cover a reprint of the energetics article from the J. Physical Chem. It probably will not be of too much use to you but I thought you might like to have it particularly since other papers which are coming out later are based on the analysis contained in it.

Give my regards to Drs. Rusch and Miller. Their recent paper in Cancer Research looks even more exciting in print than the verbal report I received when I was up your way.

Sincerely yours,

S. Spiegelman

SS/mak